



لجان الدفوعات

DISPENSING



MORPHINE ACADEMY

MORPHINE
ACADEMY

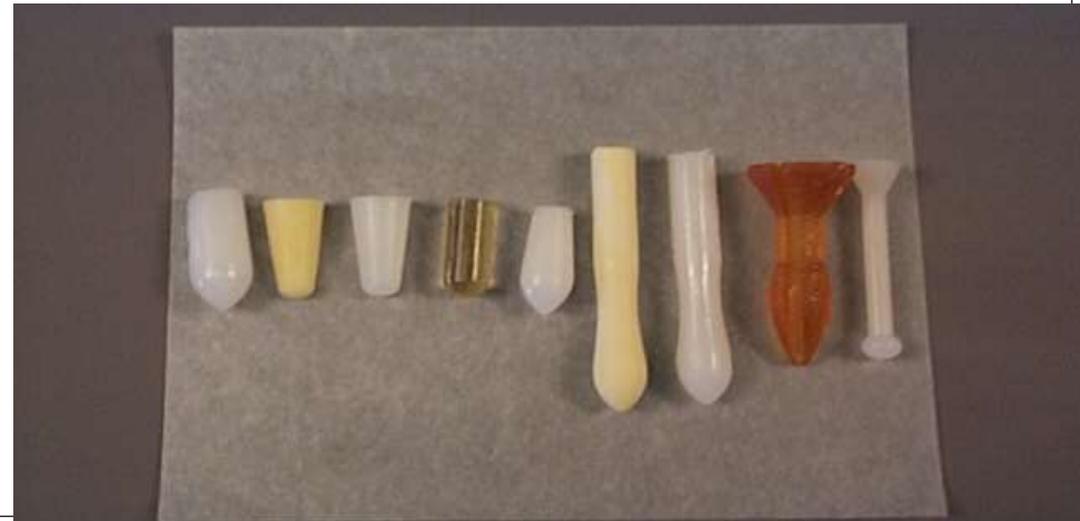
Suppositories

Introduction

- Medicated semisolid formulation that are inserted into body cavities
- Once inside cavity they melt, soften, or dissolve, releasing the drug
- For local effect (soothing inflammed hemorrhoidal tissues and promoting relaxation and evacuation)
- and for systemic effects (to treat asthma, nausea, motion sickness, anxiety...etc)
- Route of administration:

- Rectal
- Vaginal
- Urethral

بجائز الجسيم



بعد تناول
الوجبة

أشياء موصى بها

أشياء يجب تجنبها

① تذوب ② تليين

لنفس صفة نجا للتحامل بدل الامتصاص او الكسولة الفوقية؟

← تميز حريف عنه استغراق مستمر او لفعل حزين ما يقترن ببلوغ مرتبه ← فالتحامل بتعيين ضمير علي.

Introduction

- Suppositories are solid dosage forms intended for insertion into body orifices where they melt, soften, or dissolve and exert local or systemic effects.

- Rectal suppositories are inserted with the fingers, but certain vaginal suppositories may be inserted high in the tract with the aid of an appliance.

- Vaginal suppositories, also called *pessaries*,

- Urethral suppositories, also called *bougies*

لنفس صفة بالاصابع

نما لبا يحتاج ادخال

Rectal Route

- Advantages of rectal route:

- For patient with nausea and vomiting

استغراق

مابقروا يوضفوا الدواء محوياً.

- For unconscious patient

غير واعيه

- Infants and small children

- No taste limitations

مشكلة الطعم او الرائحة من موصولة لانه اصل ما يتبلع :
مشكلة الطعم او الرائحة من موصولة لانه اصل ما يتبلع :

- Partial avoidance of hepatic first-pass metabolism

بعد فتره تجاوز حيزي المرور الكيمو الكولي
First-pass

- Drugs avoid gastric fluid and enzymes

الموا مابقروا لا لحي فتره المعدة لا لانزيماتها.

Rectal Route

- Disadvantage of this route:
 - Absorption may be interrupted by defecation
 - Has small surface area for passive absorption (Drug absorption is less extensive and slower than after oral administration: SA of rectal mucosa is 1 / 10,000 the SA of small intestine)
 - Small rectal fluid content may cause problems with drug dissolution and absorption
- ⊖ Inconvenient
 - Rectal absorption of most drugs frequently is erratic and unpredictable
 - Some suppositories "leak" or are expelled after insertion

إذا صار من تعوف
ليوقف

by defecation

Drug absorption is less extensive and slower than after oral administration: SA of rectal mucosa is 1 / 10,000 the SA of small intestine)

Small rectal fluid content may cause problems with drug dissolution and absorption

كمية السائل قليلة ← ممكنة سبب صعوبة الذوبان الدواء

⊖ Inconvenient

ع: ثابت

Rectal absorption of most drugs frequently is erratic and unpredictable

ع: متغير

Some suppositories "leak" or are expelled after insertion

تفريغ

تسبب بعد الإدخال

Rectal Route

- Most commercially prepared rectal are torpedo-shaped
- 20 mm in length and weigh about 2 gm
- Infant rectal suppositories are half the size of adult suppositories
اصف اول عجز
- The maximum amount of solid material that can be incorporated into a suppository is about 30% of the blank weight
30% = اقصى الكمية التي يمكن ان تحتويها الصيغة الفارغة
- Thus, doses greater than 500 mg cannot be delivered with rectal suppositories but can be administered easily with vaginal suppositories



Rectal Route

- The factors that affect rectal absorption of a drug may be divided into two main groups:
 - (a) *physiologic factors and*
 - (b) *physicochemical factors of the drug and the base.*

Physiologic Factors

مستوى القولون.

- Colonic Content

مقام الدواء المصورة

- Circulation Route

الموصلة وحدهم وجود عدة تنظيمية للعائل

- pH and Lack of Buffering Capacity of the Rectal

Fluids: Because rectal fluids are essentially neutral in pH and have no effective buffer capacity, the form in which the drug is administered will not generally be chemically changed by the environment.

physicochemical factors of the drug and the base

كل ما كان الدواء قابلاً للدواء يجعله أفضل في الامتصاص او الماء ← الامتصاص أسرع

- relative solubility of the drug in lipid and in water

- and the particle size of a dispersed drug. → جسيمات أصغر ← تروبي أسرع ← امتصاص أسرع

مقاومة
القوة
الامتصاص

- Physicochemical factors of the base include its ability to melt, soften, or dissolve at body temperature, its ability to release the drug substance, and its hydrophilic or hydrophobic character

- The rate limiting step is the drug partitioning and diffusing out of the base material in rectal lumen

عليه انت، الدواء من Base في rectally قابلاً في المرحلة لامتصاص

Vaginal Route of Administration:

Advantages:

- Generally there is less drug degradation via this route of administration compared to oral administration. *أقل تدهوراً لتأثير الدواء مقارنة بالاقتران الفموي.*
- The dose can be retrieved if necessary. *يمكن سحب الجرعة إذا لزم الأمر.*
- Potential of long term drug administration with various intrauterine device (IUDs). *إمكانية الإعطاء طويل الأمد باستخدام أجهزة مثل IUD.*

Disadvantages:

- Absorption can be variable because vagina is a physiologically and anatomically dynamic organ. *متغير ثابت*

Retention of some delivery systems during menstruation could dispose the patient to toxic shock syndrome. *إتساءل عن الحصة*

- Can interface with sexual activity
- Can be expelled

يمكن تفرغ بسهولة.

Vaginal Route of administration

- Vaginal suppositories ^{used as!} ^{مواد حمل} are employed as: contraceptives, feminine hygiene antiseptics, antibiotics

• Vaginal suppositories = pessaries

- forms:
- Globular or oviform or cone-shaped and weigh 3-5 gm

• Inserted high in the tract with the aid of a special applicator

• Patient should be instructed to dip the suppository quickly in water before insertion

• Women should wear a sanitary napkin to protect nightwear and bed linens

تعليمات
مريض

تدريجياً في الماء قبل الإدخال.

الإعطاء

Urethral Route of Administration

Bougies

مخدرات موضعية

uses:

- Antibacterial, local preparative anesthetics
- Urethral suppositories are not specifically described in the USP 24/NF19 either by weight or dimension.
- Traditionally, they are cylindrical in shape (3 - 6 mm in diameter) and vary in length according to gender.
 - Female urethral suppositories can be 25 - 70 mm in length while male urethral suppositories can be about 50 - 125 mm in length.
- The one commercially available urethral suppository is actually marketed as a "pellet," and is 1.4 mm in diameter and 3 or 6 mm in length depending on strength.
- Urethral suppositories are unusual and may not be encountered in a compounding practice.

شكل تجاري

صغيرة الحجم

← هذه هي الطريقة التي يتم بها إعطاء الدواء عن طريق المهبل

Suppository Bases:

- Classified by composition and physical properties:

- Oleaginous (fatty) bases (رهنية / الزيتية)
- Water soluble or miscible bases → قابلية للاندماج مع الماء أو مختلفة مع الماء.



- Ideal properties:

- Nontoxic

- Nonirritating

- Inert (حاملة كيميائية)

- Compatible with the drug (متوافقة مع الدواء)

- Easily pliable into the desired shape (سهولة التشكيل بالشكل المطلوب)

- it should remain solid at room temperature but soften, melt, or dissolve readily at body temperature so that the drug is fully available soon after insertion

← لازم تكون صلبة عند 25°C، لينتشر في موقع الدواء - يتفك بعد الإدخال

- Should dissolve or melt in the presence of mucous secretions at body temperature and allow release of the drug

← لازم انها تتدوب او تذيب مع الإفرازات المخاطية - عند تيم انكسار الدواء بالكلية

Oleaginous bases

- ^{لينة} Mild and nonirritating action on the rectal mucosa
- Have a tendency to melt in 3 to 7 minutes so the drug can be released quickly from the formulation
- Have a lower melting points than the water miscible bases → must be kept in controlled room temperature environments or refrigerated in warmer climates
يجب حفظها في برودة درجة حرارة الغرفة المحفوظة أو تبريدها في المنفذ الباردة.
- e.g. Cocoa butter (Theobroma oil) and synthetic triglyceride mixtures.
بمادة صلبة ثلاثية الجلسيرات صناعية.

Cocoa Butter (Theobroma Oil)

- Cocoa Butter, NF, is defined as the fat obtained from the roasted seed of Theobroma cacao.

دهون مستخرجة من
بذور الكاكاو المحمص.

- At room temperature, it is a yellowish-white solid having a faint, agreeable chocolate-like odor.



- **Theobroma Oil** or **cocoa butter** is used as a suppository base because, in large measure, it fulfills the requirements of an ideal base.

لا يشق جعله صلباً في درجة حرارة الجسم.

Cocoa Butter (Theobroma Oil)

- At ordinary room temperatures of 15° to 25°C (59° to 77°F), it is a hard, amorphous solid, but at 30° to 36°C it melts to a bland, nonirritating oil. Thus in warm climates, theobroma oil suppositories should be refrigerated.

في المناخات الحارة، يُفضل تبريد الشمع الكاكاو.

- Thus it melts just below body temperature and yet maintaining its solidity at usual room temperatures

Cocoa Butter (Theobroma Oil)

- Particular attention must be given to two factors when preparing suppositories with cocoa butter base:
 - First, this base must not be heated above 35°C (95°F) because cocoa butter is a polymorphic compound with four structural forms and if overheated will convert to a metastable structure (alpha crystals) that melts in the 25° to 30°C (77° to 86°F) range. Thus, the finished suppositories would melt at room temperature and not be usable.

لا يُسمح برفعها فوق 35°C ← هذه زبدة الكاكاو مركب متعدد الأشكال (Polymorphic)، وقد تتحول إلى شكل غير مستقر (α crystals) بزيادة 25°-35° ← السهولة تفرغ غير صالحة عند درجة حرارة الغرفة.

- The second factor is the change in melting point caused by adding certain drugs to cocoa butter suppositories. For example, chloral hydrate and phenol tend to lower the melting point. It may be necessary to add **spermaceti or beeswax** as a hardening or solidifying agents to raise the melting point of finished suppositories back to the desired range.

تأثير الأدوية المختلفة على نقطة الانصهار : بعض الأدوية مثل chloral hydrate و phenol تقلل نقطة الانصهار ← مثل نقطة الانصهار ← مضافتة بـ spermaceti أو Beeswax لرفع نقطة الانصهار.

مراقبة النولان الصحية

Cocoa Butter (Theobroma Oil)

استخدام حمام مائي أو لوح ساحة عند 55° ← النولان الجيد.

1. The proper method of melting cocoa butter is to use a hotplate or water bath (just warm water) at about 55°C and melt the base carefully

المظهر المعتاد للنولان: كريمي + opalescent

2. Correctly melted cocoa butter should have an opalescent, creamy appearance

3. Cocoa butter that has been overheated will change to clear golden liquid and should not be used

إذا أصبح السائل شفافاً ذهبياً ← هذا نتيجة سوء جودة إزالة الشحوم عند استخدامه.

Synthetic triglycerides

تتكون من زيوت نباتية هيدروجنة

- **Synthetic triglycerides** consist of hydrogenated vegetable oils.
- Their advantage over cocoa butter is that they do not exhibit polymorphism. They are, however, more expensive.
أفضل من الشوكولاتة
الزبدة
- Some of the bases are single entity formulations. Some of the names may denote a series of bases. In a series, the bases are varied to give a range of melting points.
- For example, Fattibase® is a single entity base that consists of triglycerides from palm, palm kernel, and coconut oils. Wecobee® is a series of bases. Wecobee FS, M, R, and S are all made from triglycerides of coconut oil. But FS has a melting point range of 39.4 to 40.5°C, M has a range of 33.3 to 36.0°C, R has a range of 33.9 to 35.0°C, and S has a range of 38.0 to 40.5°C.
- Other triglyceride type bases include Dehydag®, Hydrokote®, Suppocire®, and Witepsol®.

Water Soluble/Water Miscible Bases

- Water soluble/water miscible bases are those containing glycerinated gelatin or the polyethylene glycol (PEG) polymers. تدوب بجائز ال rectal مبتدرة مختلف الدهون الي ما يتدوب عن الجراف.
- These bases dissolve in rectal mucosal fluids in contrast to triglycerides which melt at body temperature. Therefore the problems of handling, storage, and shipping are simplified. المعالج
- The glycerinated gelatin base is slower to soften and mix with the physiologic fluids than is cocoa butter and therefore provides a slower release. تدوب ببطء ← الاملاء انبعاث للدواء.

Glycerinated
gelatin

في وصفية:

Glycerinated Gelatin

- 1 • Because glycerinated gelatin-based suppositories have a tendency to absorb moisture as a result of the **hygroscopic** nature of glycerin, they must be protected from atmospheric moisture and must be kept in well-closed containers in a cool place since they will absorb and dissolve in atmospheric moisture.

لأنهم صابون في الرطوبة الجوية وتتمزج بمواد مغلقة بكمية باردة. #

- 2 • As a result of the hygroscopicity of the glycerin, the suppository may also have a dehydrating effect and irritate the tissues upon insertion.

لأنها صابون في الأجزاء ← إلى أنسجة وتؤدي إلى تهيج الغشاء المخاطي.

Glycerinated Gelatin

مادة تذيب الشحوم
بالإضافة إلى الأضداد لتقليل التهيج.

- 3 • Thus glycerin contributes to the laxative effect of the suppository by drawing water from the intestine and from its irritant action on the mucous lining
- 4 • The water in the formula for the suppositories minimizes this action; however, if necessary, the suppositories may be moistened with water prior to insertion to reduce the initial tendency of the base to draw water from the mucous membranes and irritate the tissues.

اختصار: إذ أن الشحوم السميكة تذيب الشحوم
لأنه الجليسيرين يقاسم الشحوم ليمتص الماء من القناة المعوية
عند الإدخال ← مما يسبب تهيج الأنسجة.

Glycerinated Gelatin

- is a useful suppository base, particularly for vaginal suppositories.
- It is suitable for use with a wide range of medicaments including alkaloids, boric acid, and zinc oxide.
- In addition, those intended for extended shelf-life should have a preservative added, such as methylparaben or propylparaben, or a suitable combination of the two.
- Glycerinated gelatin suppositories are translucent, resilient, gelatinous solids that tend to dissolve or disperse slowly in mucous secretions to provide prolonged release of active ingredients.

مناسب للاستخدام مع الأدوية متنوعة: \rightarrow

11

2

3

العوامل طويلة الأمد التي لها تأثيرها - يجب إضافة مادة صافية \leftarrow

سقايف

مطاطي

تتبع الأمانة المطلوب للدواء.

طريقة التحضير

Glycerinated Gelatin

- Glycerinated gelatin suppositories may be prepared by dissolving granular gelatin (20%) in glycerin (70%) and adding water or a solution or suspension of the medication (10%)
- The glycerin and water are mixed and heated (^{حمام بخار} steam bath or a boiling water bath). Then the gelatin is added slowly with gentle mixing so air is not entrapped in the mixture

للجنيب دخول الهواء



Polyethylene Glycol Polymers

- They are chemically stable, nonirritating, miscible with water and mucous secretions, and can be formulated, either by molding or compression, in a wide range of hardness and melting point.
- Certain polyethylene glycol polymers may be used singly as suppository bases but, more commonly, formulas call for compounds of two or more molecular weights mixed in various proportions as needed to yield a finished product of satisfactory hardness and dissolution time.
- Since the water miscible suppositories dissolve in body fluids and need not be formulated to melt at body temperature, they can be formulated with much higher melting points and thus may be safely stored at room temperature.

بعض أشكالها كقائمة مزيجية لوصف أنواع مختلفة من المواد
مزيجية الحصول على الصلابة المطلوبة ووقت الذوبان المناسب.

الاحتياج للنوع من حرارة الجسم ← يتم صياغتها بقطر الصغار
المنخفضة من درجة حرارة الغرفة.

التركيب الكيميائي

Polyethylene Glycol Polymers



- Polyethylene glycols are polymers of ethylene oxide and water prepared to various chain lengths, molecular weights, and physical states.
- They are available in a number of molecular weight ranges, the most commonly used being polyethylene glycol 300, 400, 600, 1,000, 1,500, 1,540, 3,350, 4,000, 6,000, and 8,000.
- The numeric designations refer to the average molecular weight of each of the polymers.
- Polyethylene glycols having average molecular weights of 300, 400, and 600 are clear, colorless liquids.
- Those having average molecular weights of greater than 1,000 are waxlike white solids whose hardness increases with an increase in the molecular weight.

متوفرة بأوزان مختلفة.

الأرقام تشير لمتوسط الوزن الجزيئي.

الوزن الجزيئي من 300 إلى 600 ← وائل عديم اللون واللون.

الوزن الجزيئي > 1000 ← صلب مثل الشمع، والصلابة تزيد مع زيادة الوزن الجزيئي.

Polyethylene Glycol Polymers

- Disadvantages of PEG bases:

- Produce **stinging or a burning sensation**
تسبب لوعة أو إحساس بالحرقان عند الإدخال.
- and may **cause a defecating reflex when used rectally** (minimized by adding water to PEG base and moistening with water before insertion)
قد تسبب تحفيز حركة الأمعاء عند الاستخدام المستقيمي من التعفّف ممكّن بإضافة الماء وتربّيبه والتحصّل قبل الإدخال.
- Polyethylene glycol suppositories that do not contain at least 20% water should be dipped in water just before use to avoid irritation of the mucous membranes after insertion. This procedure prevents moisture being drawn from the tissues after insertion and the stinging sensation.
التواصل الذي يحتوي على أقل من 20% ماء من الأهمّ تنفّس بالهواء قبل الأستخدام لتجنّب سحب الرطوبة من الأنسجة العظيمة وجفونها. أنصت باللوعة.
- **Incompatible with large number of drugs (i.e. aspirin...)**
- Should not be stored in polystyrene vials because PEG reacts with the polystyrene
عسفي تخزنها بنجاجان بوليستيرين لأنها تتفاعل معه.

Similarities between glycerinated gelatin and PEG bases

الأشبه بهم من 30 إلى 50 دقيقة حتى يذوبوا ← إطلاقه صغائر الدواء مقارنة بزيادة التكاليف.

1. They both dissolve in about 30 to 50 minutes, providing a more prolonged release of drug than cocoa butter
2. Both should be moistened with water before insertion
3. They do not melt in the fingers while being inserted
4. They do not leak from body orifices

لا يتم تذويبها بالماء قبل الإدخال.

لا تذوب في الأصابع أثناء الإدخال.

لا تسرب من فتحات الجسم

النوع	أمثلة	الخصائص	المميزات	العيوب	ملاحظات خاصة
Oleaginous (Fatty) Bases	Cocoa Butter (Theobroma oil), Synthetic triglycerides	- صلبة بدرجة الغرفة - تذوب عند حرارة الجسم (30-36°C)	- غير مهيجة - ذوبان سريع (3-7 دقائق)	- لا تتحمل الحرارة (تفسد بسرعة) - مشكلة في تعدد الأشكال (Polymorphism) - تحتاج تخزين مبرد	تستعمل غالبًا للأدوية سريعة التحرر
Glycerinated Gelatin	Glycerin + Gelatin + ماء	- تمتص الماء ببطء - لا تذوب عند حرارة الجسم بل تتحلل تدريجيًا	- تحرر دواء مطول (30-50 دقيقة)	- مهيجة للأنسجة - تسحب الماء من الأغشية المخاطية → تسبب جفاف وحرقة	يجب ترطيبها بالماء قبل الاستعمال + تبطن بوسادة صحية
Polyethylene Glycol (PEG) Bases	PEG 300, 400, 600 (سائل) PEG 1000-8000 (صلب)	- بوليمرات مستقرة - صلبة أو سائلة حسب الوزن الجزيئي - لا تحتاج حرارة الجسم للذوبان → تذوب تدريجيًا	- تخزين آمن بدرجة الغرفة - لا تذوب في الأصابع - لا تتسرب من الفتحات	- قد تسبب لسعة/حرقان - قد تحفز التبرز - غير متوافقة مع بعض الأدوية (مثل Aspirin) - تتفاعل مع عبوات البوليستيرين	يجب ترطيبها بالماء قبل الإدخال إذا احتوت >20% ماء
Water-Soluble/Miscible (عامة)	Glycerinated Gelatin, PEG	- قابلة للذوبان بالماء - لا تحتاج حرارة الجسم للذوبان	- تعطي إطلاق دواء مطول	- قد تكون مهيجة + تحتاج ترطيب	أكثر أمانًا للتخزين مقارنة بالدهني

Methods of Preparation of Suppositories:

1. Hand Rolling

- is the oldest and simplest method of suppository preparation and may be used when only a few suppositories are to be prepared in a cocoa butter base.

ما بنتائج نحسب (معملاً) الكاكاو يتحول لسكر من مذبذب لو ستمناه كثير

- It has the advantage of avoiding the necessity of heating the cocoa butter.

- A plastic-like mass is prepared by trituration grated cocoa butter and active ingredients in a mortar. The mass is formed into a ball in the palm of the hands, then rolled into a uniform cylinder with a large spatula or small flat board on a pill tile. The cylinder is then cut into the appropriate number of pieces which are rolled on one end to produce a conical shape.

متكافئ ← صوب تحسب في جرحان دسمة، ورا كذا من داتها منتظم.

Methods of Preparation of Suppositories:

2. Compression

هنا الطريقة بتخمس المتاحيل بالضغط في قالب خاص.

- is a method of preparing suppositories from a mixed mass of grated suppository base and medicaments which is forced into a special compression mold.

منه بخلاف القاعة المستوية مع المادة الدوائية ويعبره ضغطها بتالي.

Compression is especially suited for making suppositories that contain heat-labile medicinal substances or a great deal of substances that are insoluble in the base.

ادوية حساسة للحرارة لانه غير مستقر

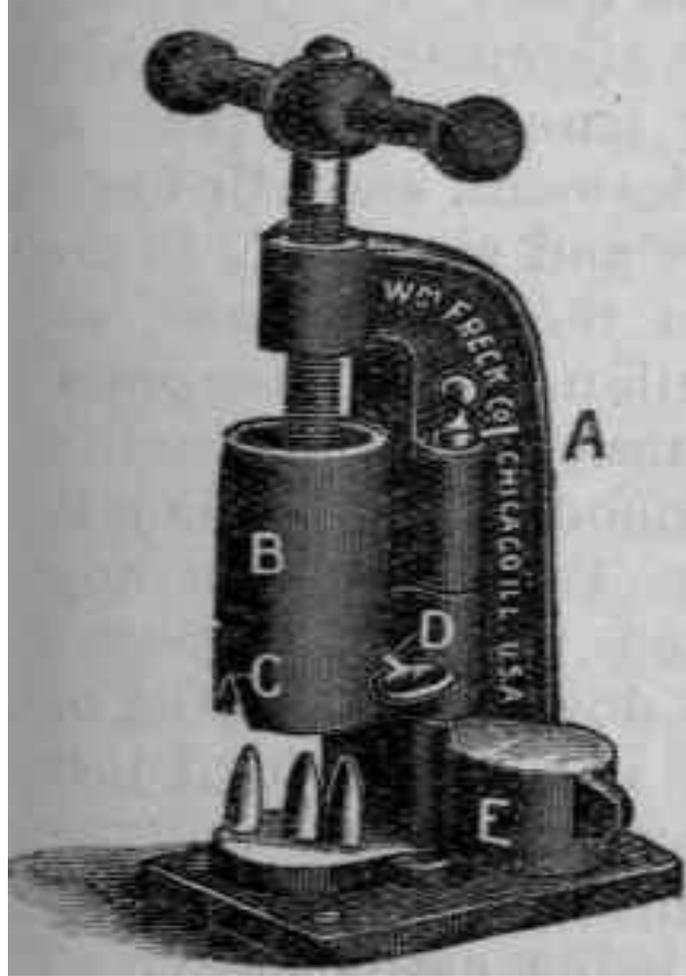
ادوية في ذائبة فالقائمة بعينها بتصل معقدة

In contrast to the molding method, **compression permits no likelihood of insoluble matter settling during manufacture.**

عاطف خطر انه المادة غير الذائبة تنسب

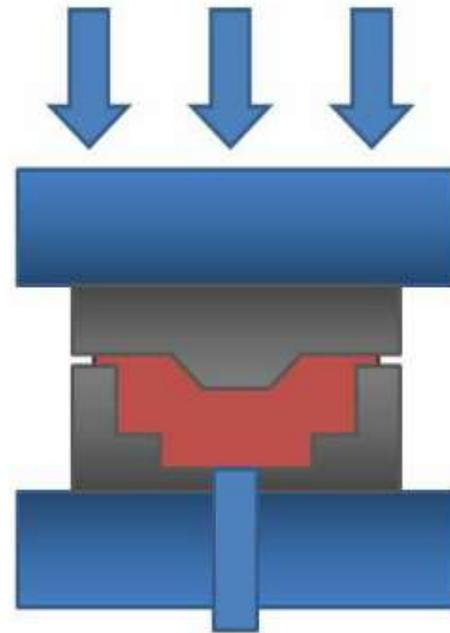
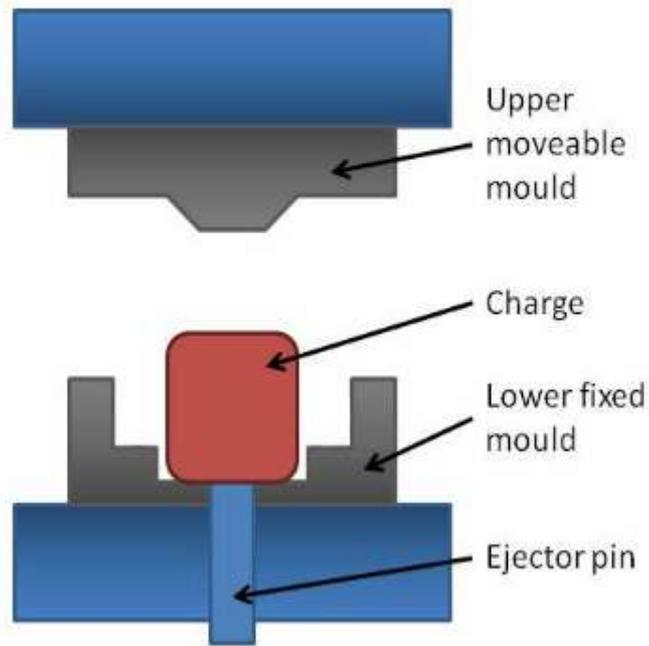
- The disadvantage to compression is that the special suppository machine is required and there is some limitation as to the shapes of suppositories that can be made.

بها طريقة خاصة + الاشكال التي بتطلع صرودة



دستگاه
سنگال
سنگال
سنگال

Compression Moulding



Methods of Preparation of Suppositories:

3. Fusion or molding

الانصهار والصب في القوالب
هذه الطريقة العكسية
حرفيا

- Cocoa butter, glycerinated gelatin, polyethylene glycol, and most other bases are suitable for preparation by molding.

- The steps in molding include (a) *melting the base*, (b) *incorporating any required medicaments*, (c) *pouring the melt into molds*, (d) *allowing the melt to cool and congeal into suppositories*, and (e) *removing the formed suppositories from the mold*..

ذوبان او ذرع المادة الغلاية فيها
P.E.G
كالكو
صبة الكلو بقوالب
اتركه يبرد ويتصلب
طلع التام من القوالب

Methods of Preparation of Suppositories:

3. Fusion or molding

- Lubrication is seldom necessary when the base is **cocoa butter** or **polyethylene glycol**, as these materials contract sufficiently on cooling to separate from the inner surfaces and allow easy removal.

مع صوكا و او PEG : غالباً حانماج تزييت القالب.

- Lubrication is usually necessary with **glycerinated gelatin**. A thin coating of mineral oil applied with the finger to the molding surfaces usually suffices.

مع الجاليرينج : لازم تزييت (مثلاً بزيت معدني)

Methods of Preparation of Suppositories:

3. Fusion

القالب

Suppository molds:

تستخدم لإنتاج مئات التماثيل دفعة واحدة.

- Industrial molds:

produces hundreds of suppository in a single batch



اصفقا
التي
تستخدم

تستخدم لإنتاج التماثيل دفعة واحدة

مجموعة بالية

- Small hand-held molds:

Are made of:

Stainless steel

Aluminum

نحاس ابيض

Brass

Plastic

مطاط

Rubber



Methods of Preparation of Suppositories:

3. Fusion or molding

- Suppositories are generally made from solid ingredients and drugs which are measured by weight.
- When they are mixed, melted, and poured into suppository mold cavities, they occupy a volume – the volume of the mold cavity.

Since the components are measured by weight but compounded by volume, density calculations and mold calibrations are required to provide accurate doses.

منه كبر حجمها

لذا حسابات دقيقة ← لانها بتوزن المواد لكن بتنكبهم بمجم القالب ← بتلازم نقل معلية قالب وكمية عالية

عزائبا

① دقة الجرعة
② مناسبة لمعظم القواعد

الطريقة	الوصف	المميزات	العيوب	متى تستخدم؟
Hand Rolling (الدرجة) باليد	خلط القاعدة (كاكاو غالبًا) مع الدواء → تشكيلها يدويًا بشكل مخروطي	- بسيطة جدًا- ما يحتاج تسخين	- مش دقيقة بالجرعة- الشكل غير منتظم- صعبة لو عدد كبير	لما يكون المطلوب عدد قليل وبقاعدة كاكاو
Compression (الضغط)	خلط القاعدة المبشورة مع الدواء → ضغطها بقالب خاص	- مناسبة للأدوية الحساسة للحرارة- تمنع ترسب المواد غير الذائبة	- بدها آلة خاصة- محدودية بالأشكال	لما يكون عندي أدوية غير ذائبة أو حساسة للحرارة
Fusion/Molding (الانصهار) والصب	إذابة القاعدة + دمج الدواء → صب في قوالب → تبريد	- دقيقة بالجرعة- تناسب معظم القواعد	- تحتاج تسخين (ممكن يفسد بعض الأدوية)- بدها معايرة قوالب وكثافة	الطريقة الأكثر شيوعًا، خصوصًا للإنتاج الكمي والصناعي

Density Factors

لما نضع دواء داخل قاعدة الشمع (زيت زبدة الكاكاو) الدواء ان يوفد مكانه من القاعدة

- When a drug is placed in a suppository base, it will displace an amount of base as a function of its density.
 بي مقدار الاذاحة يعتمد على كثافة الدواء مقارنة بكثافة القاعدة.

1. If the drug has the same density as the base, it will displace an equivalent weight of the base.
 ان يخرج نفس الوزن المصنوع

2. If the density of the drug is greater than that of the base, it will displace a proportionally smaller weight of the base.
 الدواء اقل

- Density factors for common drugs in cocoa butter are available in standard reference texts.
 ان يخرج وزنه اقل من القاعدة.

3. اذا كانت كثافة الدواء اقل من وزنه اكبر من القاعدة.

Density Factors:

- The density factor is used to determine how much of a base will be displaced by a drug. The relationship is:

$$\text{Density Factor} = \text{Weight of drug} / \text{Weight of base displaced}$$

- For example: Aspirin has a density factor in cocoa butter of 1.3. If a suppository is to contain 0.3 g of aspirin, it will replace $0.3 \text{ g} \div 1.3$ or 0.23 g of cocoa butter. If the blank suppository (suppository without the drug) weighed 2 g, then $2 \text{ g} - 0.23 \text{ g}$ or 1.77 g of cocoa butter will be needed for each suppository, and the suppository will weigh $1.77 \text{ g} + 0.3 \text{ g} = 2.07 \text{ g}$. So if a pharmacist was making 12 aspirin suppositories using cocoa butter as the base, he would weigh $1.77 \text{ g} \times 12$ or 21.24 g of cocoa butter and $0.3 \text{ g} \times 12$ or 3.6 g of aspirin.



مثال (البروموزين الكالسيوم)

$$* \text{ لو النسبة الناتجة وزنها } = 2g$$

$$\leftarrow \text{ القاسم المطلوب } = 2 - 0.23 = 1.77g$$

$$\leftarrow \text{ الوزن النهائي للنسبة } = 0.3 + 1.77 = 2.07g$$

$$\text{معامل الكفاءة (DF)} = 1.3$$

$$\text{الكمية المراد إضافتها} = 0.3g$$

$$\text{الأحقة} = \frac{0.3}{1.3} = 0.23g \text{ من الكالسيوم بوزن.}$$

لو برمي أعلى 12 كجم :

$$\bullet \text{ كجم القاسم } = 12 * 1.77 = 21.24g$$

$$\bullet \text{ كجم الـ 8 بروموزين } = 12 * 0.3 = 3.6g$$

Density Factors:

- Some example density factors of drugs in cocoa butter are shown in the table below (*see Remington's*) also see Table 17.4 pg 138

Aspirin	1.3
Barbital	1.2
Bismuth salicylate	4.5
Chloral hydrate	1.3
Cocaine hydrochloride	1.3
Codeine phosphate	1.1
Diphenhydramine hydrochloride	1.3
Morphine hydrochloride	1.6
Phenobarbital	1.2
Zinc Oxide	4.0

When the Density Factor is Not Known

- When bases other than cocoa butter are used, or when the density factor for a drug in cocoa butter is not known, then the density factor can be **estimated by calculation** or experimentally determined by the **double casting technique**.

الكمية الفارغة.

اصبه بالتبريد.

- The weight of the **blank suppository** is easily determined. A portion of the suppository base is melted, poured into the suppository mold and allowed to congeal. The suppositories are removed from the mold, and the total weight of the suppositories is determined. The average weight of the blank suppository is determined by dividing the total weight by the number of suppositories.

① تصيب كمية من القاعدة . ② تبريدها وتبقيها بالقالب . ③ يتركها ليبرد congeal .

④ بعد ذلك يقطع كل القاصيل من القالب . ⑤ توزنهم كلهم و ← هذا الوزن الكلي . ⑥ تقسم الوزن الكلي = الوزن المقطوع للكمية الفارغة الواحدة .
عدد القاصيل



مثال صغیر ↑ :



لو صبیبت قاصده PEG ری قالب و طلعی 6 حاصل . وزن تمام ~~کلم~~ = 12g

∴ العزیه الکلی = 12g

عدد التامیل = 6

العزیه السوے للحصه الفارسیه = $\frac{12g}{6} = 2g$ کل حصه فارسیه .

#

When the Density Factor is Not Known:

A. Estimation by Calculation

- One method to determine the density factor of a drug in a base other than cocoa butter requires the use of the ratio of a blank suppository of the non-cocoa butter base to a blank suppository of the cocoa butter base. This information is generally obtained by calibrating the mold first with one base and then the other base.
- As an example of the method, a mold was calibrated with the PEG base and the average blank suppository weighed 2.24 grams. The same mold was calibrated with cocoa butter and those blank suppositories weighed 1.87 grams on average. Therefore, the ratio of the two weights was:

$$\frac{\text{weight of PEG suppositories}}{\text{weight of cocoa butter suppositories}} = \frac{2.24 \text{ g}}{1.87 \text{ g}} = 1.20$$

When the Density Factor is Not Known:

A. Estimation by Calculation

- If 200 mg of aspirin is to be incorporated into each PEG suppository, it is necessary to determine how much PEG base will be displaced by the aspirin. That displacement amount can be calculated as follows:
 - density factor of aspirin in cocoa butter = 1.3 (from reference sources)
 - density of PEG base relative to cocoa butter = 1.20 (the ratio obtained from the calibrations)
 - 0.2 g of aspirin will displace $\frac{0.2 \text{ g}}{1.3} \times 1.20 = 0.18 \text{ g}$ of PEG base
- For each PEG suppository to be formulated, 0.2 g of aspirin and 2.06 g ($2.24 \text{ g} - 0.18 \text{ g} = 2.06 \text{ g}$) of the PEG base will be needed

لغاير نفس القالب لبقا من نبيذ مستعملت (مثل PEG و cocoa butter)

* مثل العجينة :

- مع 2.24g = PEG العجينة الفارغة

- مع 1.87g = cocoa butter العجينة النازحة

$$\therefore \text{نسبة الكثافة النسبية} = \frac{2.24}{1.87} \approx 1.2$$

لتقدير لزوجة PEG لدينا نعرف DF
أبدا بالأكالو :

$$\text{لدينا} \rightarrow \text{DF} = 1.3$$

لدينا نعرف 0.2g + بربيه في PEG :

$$\text{وزن الزيادة الأكالو} = \frac{0.2}{1.3} = 0.154$$

$$\text{وزن الزيادة PEG} = \frac{0.154}{1.2} \approx 0.18$$

∴ كل لحصة PEG، نحتاج : $2.24 - 0.18 = 2.06g$

قائمة PEG + 0.2g
الزيادة

#

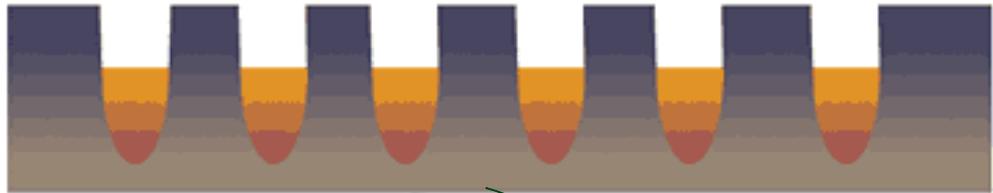
When the Density Factor is Not Known:

A. Double Casting Technique

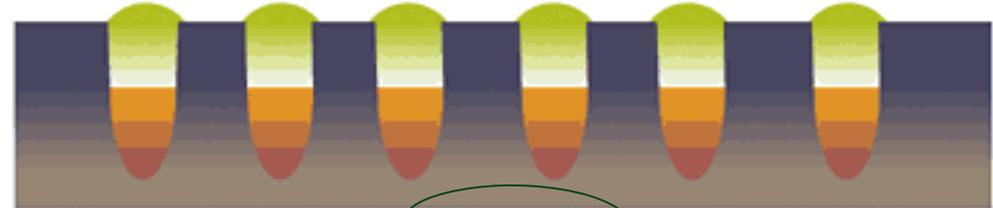
- By determining the weights of suppositories at the various steps the density factor can be calculated.

- The double casting techniques can be used to determine the density factor of any drug in any base

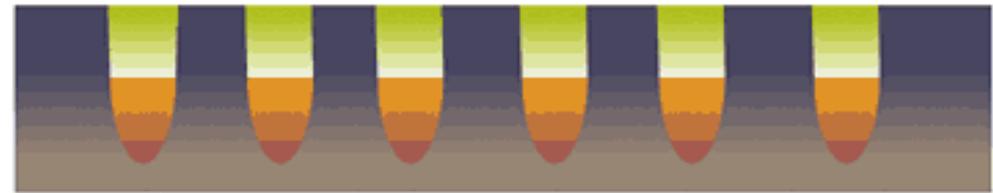
Double Casting Method of Suppository Preparation



1. Mix all of the drug with a portion of the base and use the mixture to partially fill each of the suppository mold cavities.



2. Use plain base to overfill each cavity.



3. Let cool, then remove excess base from top of mold. Remove suppositories, remelt, and recast to evenly distribute the drug.

When the Density Factor is Not Known:

A. Double Casting Technique

تعريف وزن التصليد القابلة من القالب (مثلاً 2.0 جم ككافو)

- Using a particular mold, the average weight of a plain cocoa butter suppository was found to be 2.0 g. Using the same mold, cocoa butter suppositories, each containing 300 mg of drug A, were found to weigh 2.1 g each. So,

- weight of suppository of cocoa butter = 2.0 g

weight of drug in each medicated suppository = 0.3 g

weight of suppository with drug and cocoa butter = 2.1 g

weight of base in medicated suppository = 2.1 g - 0.3 g =

1.8 g

weight of base displaced = 2.0 g - 1.8 g = 0.2 g

الوزن القابلة
المنزاحة

Therefore, density factor of drug A = $0.3 \text{ g} \div 0.2 \text{ g} = 1.5$

DF
للدواء A

وزن القالب في
التصليد البترواوية

$$DF = 1.5$$

وزن الدواء لكل حبة = 0.3 g

وزن الحبة الفارغة (أو الكاف)
لحبات 10 = العدد

- Homework?

Using the density factor determined above, how much cocoa butter and drug A are needed to make 10 cocoa butter suppositories each containing 0.3 gm of drug?

$$\text{Base displaced} = \frac{0.3}{1.5} = 0.2 \text{ g} \quad \rightarrow \text{القياسية المضافة لكل حبة}$$

$$2 - 0.2 = 1.8 \text{ g} \quad \rightarrow \text{كمية القياسية الباقية لكل حبة}$$

$$\begin{array}{l} \text{الدواء} : 0.3 \times 10 = 3 \text{ g} \\ \text{القابض} : 1.8 \times 10 = 18 \text{ g} \end{array} \quad \rightarrow \text{المجموع لكل 10 حبات}$$

$$1.8 + 0.3 = 2.1 \text{ g} \quad \rightarrow \text{الوزن النهائي لكل حبة واحدة.} \quad \#$$

سؤال يد - حجم فيج الأفكار التي يمكن تيجي مع التماسيل:

القاعدة المزاحة (نفس القاعدة):

$$\text{Base disp.} = \frac{W_{\text{drug}}}{DF}$$

نقل الإزاحة لقاعدة أخرى (Ratio):

$$\text{Base disp. (new)} = \left(\frac{W_{\text{drug}}}{DF_{\text{cocoa}}} \right) \times \text{Ratio}$$

$$\text{Ratio} = \frac{W_{\text{blank (new base)}}}{W_{\text{blank (cocoa)}}$$

DF بالتجربة (Double Casting):

$$DF = \frac{W_{\text{drug}}}{(W_{\text{blank}} - W_{\text{base in medicated}})}, \quad W_{\text{base in medicated}} = W_{\text{medicated}} - W_{\text{drug}}$$

القاعدة المطلوبة/وحدة:

$$W_{\text{base needed}} = W_{\text{blank}} - W_{\text{base displaced}}$$

الوزن النهائي/وحدة:

$$W_{\text{final}} = W_{\text{base needed}} + W_{\text{drug}}$$

① احس كمية القاعدة والمواد لصنع عدد محدد من التماسيل.

② إذا تغيرت القاعدة (PEG بن cocoa butter)، عدّل الحساب باستخدام (ratio) حيث

③ إذا أعطاك بيانات double casting، اخرج DF أولاً.

④ مثال عريض: يعطيان DF والوزن النهائي للتمهيلة ← اخرج وزن الدواء أو القاعدة.

⑤ معادلة: أي دواء نخرج كمية أكبر/أصغر من القاعدة هي كالتالي.

A pharmacist wants to prepare 10 cocoa butter suppositories, each containing 0.3 g of aspirin. The density factor (DF) of aspirin in cocoa butter is 1.3, and the blank suppository weighs 2.0 g.

- Calculate the amount of cocoa butter required for the batch.
- Calculate the total weight of aspirin required.

$$* \text{ Base displaced} = \frac{\text{weight of drug}}{DF} = \frac{0.3}{1.3} \approx 0.231 \text{ g}$$

$$* \text{ cocoa butter needed} = \text{Blank suppository} - \text{Base displaced} = 2 - 0.231 \approx 1.769 \text{ g}$$

$$* \text{ total aspirin for 10 suppositories} \rightarrow 0.3 \times 10 = 3 \text{ g}$$

cocoa butter = 17.7g Aspirin = 3g

#

A pharmacist wants to prepare PEG suppositories containing 0.2 g of aspirin per suppository. A mold was calibrated with PEG and the average blank PEG suppository weighs 2.24 g. The same mold calibrated with cocoa butter gives average blank cocoa butter suppositories weighing 1.87 g. The density factor of aspirin in cocoa butter = 1.3.

Calculate:

- How much PEG base is displaced by aspirin per suppository.
- The amount of PEG base needed per suppository.
- Total PEG and aspirin required for 10 suppositories.

$$* \text{ ratio of PEG to cocoa butter} = \frac{2.24}{1.87} \approx 1.2$$

$$* \text{ Base displaced (PEG)} = \frac{\text{weight of drug}}{DF_{\text{cocoa}}} \times \text{Ratio} = \frac{0.2}{1.3} \times 1.2 \approx 0.185 \text{ g}$$

$$* \text{ PEG base required per suppository} = \text{Blank PEG} - \text{Base displaced} = 2.24 - 0.185 \approx 2.055 \text{ g}$$

$$* \text{ Total quantities for 10 suppositories: PEG} = 2.055 \times 10 = 20.55 \text{ g}, \text{ Aspirin: } 0.2 \times 10 = 2 \text{ g} \quad \#$$

Using a cocoa butter mold, the average blank suppository weighs 2.0 g. Suppositories containing 0.3 g of Drug A weigh 2.1 g each.

Calculate:

- The density factor (DF) of Drug A in cocoa butter.
- The amount of cocoa butter and Drug A required to prepare 10 suppositories.

$$* \text{ weight of base in medicated suppository} = 2.1 - 0.3 = 1.8 \text{ g}$$

$$* \text{ Base displaced} = 2 - 1.8 = 0.2 \text{ g}$$

$$* \text{ DF} = \frac{\text{weight of drug}}{\text{Base displaced}} = \frac{0.3}{0.2} = 1.5$$

$$* \text{ cocoa butter per suppository} = 2 - 0.2 = 1.8 \text{ g}$$

$$* \text{ Total quantities for 10 suppositories} \rightarrow \text{cocoa butter: } 1.8 \times 10 = 18 \text{ g} \quad \{ \text{drug A: } 0.3 \times 10 = 3 \text{ g} \quad \#$$

#

A prescription calls for 5 suppositories containing 0.4 g of paracetamol each. The blank cocoa butter suppository weighs 2.5 g, and the density factor (DF) for paracetamol = 1.2.

Calculate:

- The amount of cocoa butter per suppository.
- Total cocoa butter and paracetamol for the batch.
- If the batch is doubled to 10 suppositories, recalculate totals.

$$* \text{ Base displaced per suppository} = \frac{0.4}{1.2} = 0.333 \text{ g}$$

$$* \text{ cocoa butter per suppository} = 2.5 \text{ g} - 0.333 \text{ g} = 2.167 \text{ g}$$

* Totals for 5 suppositories:

$$\begin{aligned} \text{cocoa butter} &: 2.167 * 5 \approx 10.835 \text{ g} \\ \text{Paracetamol} &: 0.4 * 5 = 2 \text{ g} \end{aligned}$$

* Totals for 10 suppositories:

$$\begin{aligned} \text{cocoa butter} &: 2.167 * 10 \approx 21.67 \text{ g} \\ \text{Paracetamol} &: 0.4 * 10 = 4 \text{ g} \end{aligned}$$

#

Packaging and Storage

الحفاظ على المنتجات بالحمامة بدرجة حرارة منخفضة لتفكيكها ببطء.

- Because suppositories are adversely affected by heat, it is necessary to maintain them in a cool place.

لو انك تتعب

- Cocoa butter suppositories must be stored below 30°C (86°F), and preferably in a refrigerator (2°C to 8°C , or 36°F to 46°F).

الحفاظ على المنتج في درجة الحرارة المنخفضة

- Glycerinated gelatin suppositories can be stored at controlled room temperature (20°C to 25°C , or 68°F to 77°F).
- Suppositories made from a base of polyethylene glycol may be stored at usual room temperatures.

Packaging and storage

لوزم بسببها

- If they must be stored in the refrigerator, suppositories should be allowed to warm to room temperature before insertion.

اذا التجمد كانت بالراحة : لازم نتركيها ترفع لدرجة الحرارة الحوية قبل الاستعمال

لعلها تكون جامدة وصعبة تظل

- The patient should be advised to rub cocoa butter suppositories gently with the fingers to melt the surface to provide lubrication for insertion.

انكاو: يرفع المرشح ليعزل المادة بأصابعه
عند نزولها يزداد رطوبتها في lubrication.

- Glycerinated gelatin or polyethylene glycol suppositories should be moistened with water to enhance lubrication.

حائض تنفك ، الافضل لترطيبها

ببسي قبل الادخال.

Packaging and Storage

- Glycerin suppositories and glycerinated gelatin suppositories are packaged in tightly closed glass containers to prevent a change in moisture content
- Suppositories stored in high humidity may absorb moisture and tend to become spongy, whereas suppositories stored in places of extreme dryness may lose moisture and become brittle.

- لو صغفناها برطوبة عالية ← بتتبدل اللي وبتعيس اغشية .

- لو صغفناها بجو جاف جدا ← بتفقد اللي وبتعيس هشة / قابلة للتشقق .

Observing formulations for evidence of instability

- Should be stored protected from heat, and may be stored under refrigeration but not frozen
- Glycerin and PEG base suppositories should be kept in airtight containers because they are hygroscopic
- Suppositories should be observed for:

تفتت / زلال - excessive softening

جفاف - Drying out

تصلب / شدة او متكسرة - Harden or shrivel

بقع / لاصق - Oil staining on the packaging

بقع / لاصق

انما خبز

VAGINAL INSERTS

- Vaginal tablets are more widely used nowadays than are commercial vaginal suppositories

جهاز بلاستيكي لتسهيل الإدخال.
 بعبوة البلاستيك

- Vaginal tablets, frequently referred to synonymously as vaginal inserts, are usually ovoid and are accompanied in their packaging with a plastic inserter, a device for easy placement of the tablet within the vagina.

- They are prepared by tablet compression and are commonly formulated to contain lactose as the base or filler, a disintegrating agent such as starch, a dispersing agent such as polyvinylpyrrolidone, and a tablet lubricant such as magnesium stearate.

حامل الدواء
 مادة ممتدة
 مادة ممتدة
 مادة ممتدة

مادة ممتدة
 مادة ممتدة

- The tablets are intended to disintegrate within the vagina, releasing their medication

العزم لتفكك ويطلق الدواء المتاح

كمان في بعض ال vaginal inserts بتكون على شكل كبسولات جيلاتينية صلبة بالدواء صلبتوب وبمقلده

Vaginal inserts

- Some vaginal inserts are capsules of gelatin containing medication to be released intravaginally.



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يعني أظننا بس هو ليس آخرنا لأنه ضائل ثابتية

واحد ورقي
والثاني videos :)

فألكم الفل جويجا - دعواتكم